Examiner's convenience. Should any discrepancies be discovered, the version presented in the preceding "IN THE SPECIFICATION" and "IN THE CLAIMS" sections shall take precedence.

These amendments are fully supported by the specification as filed and do not constitute new matter. The amendment to αMSHR Forward Primer 1 as shown in the text beginning at page 19, line 31 and ending at page 20, line 5 is supported *inter alia* page 28 and claim 46. The amendment to the Meishan and Wild Boar sequences as shown in the paragraphs beginning at page 68, line 22 and ending at page 68, line 34 is supported *inter alia* Figure 1a.

The Notice to Comply mailed December 1, 2000 for the above-identified application alleges that the application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825. Applicants submit herewith a Substitute Sequence Listing in paper and computer readable form. The content of the paper and computer readable copies of the Substitute Sequence Listing submitted in accordance with 37 C.F.R. §1.821(c) and (e) are the same and do not include new matter. An amendment to Figure 1 will be made at a later date in order to bring it in conformity with the Substitute Sequence Listing.

Applicants have enclosed the fee required for a five-month extension of time pursuant to 37 C.F.R. §1.17(a)(5). Please charge any additional fee associated with this filing or credit any overpayment to Deposit Account No. 02-4377. Two copies of this paper are enclosed.

A copy of the Notice to Comply is enclosed.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE SPECIFICATION

The paragraph beginning at page 19, line 31 and ending at page 20, line 5 has been amended as follows:

αMSHR **Forward Primer 1**: (5'-TGT AAA ACG ACG GCC AGT RGT GCC TGG AGG TGT CCA T-3')(Sequence ID No. 1)

αMSHR **Reverse Primer 5**: (5'-CGC CCA GAT GGC CGC GAT GGA CCG-3')(Sequence ID No. 2); or

αMSHR **Forward Primer 2**: (5'-CGG CCA TCT GGG CGG GCA GCG TGC -3')(Sequence ID No. 3)

αMSHR **Reverse Primer 2**: (5'-GGA AGG CGT AGA TGA GGG GGT CCA-3')(Sequence ID No. 4); or

αMSHR **Forward Primer 3**: (5'-GCA CAT CGC CCG GCT CCA CAA GAC-3')(Sequence ID No. 5)

αMSHR **Reverse Primer 3**: (5'-GGG GCA GAG GAC GAC GAG GGA GAG-3')(Sequence ID No. 6).

The paragraph beginning at page 24, line 8 and ending at page 24, line 8 has been amended as follows:

LA93 5' – GAGCAGCCCCTACCCCGGAATGCCAGTTGA – 3' (Sequence ID No. 7)

The paragraph beginning at page 24, line 10 and ending at page 24, line 11 has been amended as follows:

KIT56 5' - CTTTAAAACAGAACATAAAAGCGGAAACATCATGCGAAGG - 3' (Sequence ID No. 8)

The paragraph beginning at page 25, line 2 and ending at page 25, line 6 has been amended as follows:

Figure 1. Partial nucleotide sequence (a) (Sequence ID Nos. 37-42) and the derived amino acid sequence (b) (Sequence ID Nos. 43-47) of the porcine aMSH-R gene as determined from a number of pig breeds. Position numbers for the nucleotide sequence are based upon nucleotide 1 being the A of the ATG initiation codon. Numbers of the amino acids are in accordance with the bovine BDF3 sequence (Vanetti *et al.*, FEBS Lett. **348**: 268-272 (1995)) to allow comparison.

The text beginning at page 27, line 1 and ending at page 27, line 3 has been amended as follows:

Figure 10: Nucleotide sequence of the porcine *KIT* cDNA from an animal of the Hamshire breed (SEQ ID NO. 47). The sequence is numbered with the first nucleotide of the N terminal methionine codon taken as 1.

The text beginning at page 27, line 13 and ending at page 27, line 18 has been amended as follows:

Nucleotide sequence of the 3' end of the porcine αMSHR coding region and adjacent 3' untranslated region. The TGA stop codon is highlighted in bold, the promer binding sites for EPIG14 is shown in italics. Numbering is based on the system used in figure 1a in which nucleotide 1 is the A of the ATG initiation codon of the Wild Boar sequence. Bases in common with the European Wild Boar are marked with a dash. Missing bases are marked with a :. The Wild Boar sequence corresponds to SEQ ID NO. 49. The Meishan and Large Black sequences correspond to SEQ ID NO. 50. The Hampshire, Pietrain, and Duroc sequences correspond to SEQ ID NO. 51.

The text beginning at page 28, line 27 and ending at page 29, line 22 has been amended as follows:

Primers MSHR Forward Primer 1: (5'-TGT AAA ACG ACG GCC AGT RGT GCC TGG AGG TGT CCA T-3')(Sequence ID No. 1); and

MSHR Reverse Primer 5: (5'-CGC CCA GAT GGC CGC GAT GGA CCG-3')(Sequence ID No. 2)

amplify a 428 bp fragment from the 5' half of the gene.

Primers MSHR Forward Primer 2: (5'-CGG CCA TCT GGG CGG GCA GCG TGC -3')(Sequence ID No. 3);

and αMSHR Reverse Primer 2: (5'-GGA AGG CGT AGA TGA GGG GGT CCA-3')(Sequence ID No. 4)

amplify a 405 bp fragment of the 3' half of the gene.

As these two fragments are non-overlapping a third primer pair

αMSHR Forward Primer 4 (5'-TGC GCT ACC ACA GCA TCG TGA CCC TGC-3')(Sequence ID No. 10); and

αMSHR Reverse Primer 4 (5'-GTA GTA GGC GAT GAA GAG CGT GCT-3')(Sequence ID No. 11)

were used to amplify a 98 bp fragment which spans the 50 bp gap. PCR was carried out on a DNA thermal cycler (Perkin Elmer 9600) in a total volume of 20 µl containing 25 ng genomic DNA, 1.0 mM ~~MgCl2~~ $MgCl_2$, 50 mM KCl, 10 mM Tris-HCl, pH 8.3, 200 ~~(M~~ µM dNTPs, 0.5 U AmpliTaq Gold (Perkin Elmer) and 10 pmol of both KIT21 and KIT35 primers. To activate AmpliTaq Gold, initial heat denaturation was carried out at ~~94 degrees~~ 94° C for 10 minutes followed by 32 cycles each consisting of 45 sec at ~~94 degrees~~ 94° C, 45 sec at ~~53 degrees~~ 53° C and 45 sec at ~~72 degrees~~ 72° C. The final extension lasted for 7 min at ~~72 degrees~~ 72° C. PCR products were cloned into vector pUC18 using the SureClone ligation kit (Pharmacia Biotech).

The paragraphs beginning at page 31, line 14 and ending at page 31, line 17 have been amended as follows:

MSHR Forward Primer 3 sequence: 5'-GCA CAT CGC CCG GCT CCA CAA GAC-3' (Sequence ID No. 5)

MSHR Reverse Primer 3 sequence : 5'-GGG GCA GAG GAC GAC GAG GGA GAG-3' (Sequence ID No. 6)

The paragraphs beginning at page 37, line 11 and ending at page 37, line 12 have been amended as follows:

Forward primer sequence: 5'-CTG CCT GGC CGT GTC GGA CCT G-3' (Sequence ID No. 12)

Reverse primer sequence: 5'-CTG TGG TAG CGC AGC GCG TAG AAG-3' (Sequence ID No. 13).

The paragraph beginning at page 39, line 8 and ending at page 39, line 9 has been amended as follows:

5'-TGAGGTAGGAGAGTTTTGGG-3' (Sequence ID No. 14)
5'-TCGAAATTGAGGGGAAGACC-3' (Sequence ID No. 15)

The paragraph beginning at page 40, line 13 and ending at page 40, line 28 has been amended as follows:

First-strand cDNA synthesis was accomplished using the First-Strand cDNA Synthesis kit (Pharmacia Biotech) so that ~100 ng mRNA was randomly primed by 0.1 μg pd(N6) in a total volume of 15 μl. Two μl of the completed first cDNA strand reaction was then directly used per 12 μl PCR reaction by adding 10 μl PCR mix containing 10 pmol each of the mouse/human derived primers KIT1F and KIT7R (5'-TCR TAC ATA GAA AGA GAY GTG ACT C-3' (Sequence ID No. 28) and 5'-AGC CTT CCT TGA TCA TCT TGT AG-3' (Sequence ID No. 29), respectively; Moller et al. 1996, *supra*), 1.2 μl 10 x PCR-buffer (10 mM Tris-HCl, pH 8.3, 50 mM KCl) and 0.5U of AmpliTaq polymerase (Perkin-Elmer) incubated with an equal amount Taqstart antibody (Clontech) at 25° C for 5 min to achieve a hot start PCR. The reaction was covered with 20 μl mineral oil and thermocycled in a Hybaid Touchdown machine (Hybaid) with 40 cycles at 94° C for 1 min, 55-48° C (touchdown one degree per cycle the first seven cycles and then 48° C in the remaining cycles) for 1 min and 72° C for 1 min. After PCR 2 μl loading dye was added to each sample which were then loaded on 4% agarose gel (Nusieve/Seakem 3:1, FMC Bioproducts) and electrophoresed with 100V for 80 min. Products were visualized by ethidium bromide staining and UV-illumination.

The paragraph beginning at page 42, line 2 and ending at page 42, line 12 has been amended as follows:

A 175 bp region including the boundary between exon 17 and intron 17 of the *KIT* gene was amplified for sequence analysis using forward primer KIT21 (5' – GTA TTC ACA GAG ACT TGG CGG C – 3')(Sequence ID No. 16) and reverse primer KIT35 (5' – AAA CCT GCA AGG AAA ATC CTT CAC GG -3')(Sequence ID No. 17). PCR was carried out on a DNA thermal cycler (Perkin Elmer 9600) in a total volume of 20 µl containing 25 ng genomic DNA, 1.0 mM $MgCl_2$, 50 mM KCl, 10 mM Tris-HCl, pH 8.3, 200 µM dNTPs, 0.5U AmpliTaq Gold (Perkin Elmer) and 10 pmol of both KIT21 and KIT35 primers. To activate AmpliTaq Gold, initial heat denaturation was carried out at 94° C for 10 minutes followed by 32 cycles each consisting of 45 sec at 94° C, 45 sec at 55° C and 45 sec at 72° C. The final extension lasted for 7 min at 72° C. PCR products were cloned into vector pUC18 using the SureClone ligation kit (Pharmacia Biotech).

The paragraph beginning at page 49, line 24 and ending at page 49, line 25 has been amended as follows:

Forward GAATATTGTTGCTATGGTGATCTCC *KIT*1-FOR (Sequence ID No. 18)

Reverse CCGCTTCTGCGTGATCTTCCTG *KIT*1-REV (Sequence ID No. 19)

The paragraph beginning at page 49, line 29 and ending at page 49, line 30 has been amended as follows:

Forward CTGGATGTCCTGTGTTCCCTGT CRC-FORWARD (Sequence ID No. 20)

Reverse AGGTTTGTCTGCAGCAGAAGCTC CRC-REVERSE (Sequence ID No. 21)

The paragraph beginning at page 53, line 15 and ending at page 53, line 17 has been amended as follows:

Forward GAAAGTGA(C/T)GTCTGGTCCTAT(C/G)GGAT *KIT*DEL2-FOR (Sequence ID No. 22)

Reverse AGCCTTCCTTGATCATCTTGTAG *KIT*DEL2-REV (Sequence ID No. 23)

The paragraph beginning at page 56, line 28 and ending at page 56, line 29 has been amended as follows:

forward TGTGGGAGCTCTTCTCTTTAGG *KIT*DEL1-FOR (Sequence ID No. 24)

reverse CCAGCAGGACAATGGGAACATCT *KIT*DEL1-REV (Sequence ID No. 25)

The paragraph beginning at page 58, line 17 and ending at page 59, line 5 has been amended as follows:

mRNA was isolated from peripherial blood leukocytes from white (Landrace/Large White) and coloured (Hampshire) pigs using the Message Maker mRNA isolation system (Gibco BRL) with one mRNA selection from total RNA. 100 ng poly(A)$^+$ mRNA was reverse-transcribed with random primers (First-Strand cDNA Synthesis kit, Pharmacia Biotech) and the product was used at a 1:10 dilution for RT-PCR using the proof-reading Advantage KlenTaq Polymerase (Clontech) according to the manufacturer's recommendation. The following primers were used to amplify almost the entire coding sequence and some of the 5' untranslated region: KIT40 (5' – GGC TCT GGG GGC TCG GCT TTG C – 3')(Sequence ID No. 26) corresponding to the untranslated region and KIT22S (5' – TCA GAC ATC TTC GTG GAC AAG CAG AGG – 3')(Sequence ID No. 27) corresponding to exon 21; both primers had been designed using consensus sequence of the human and mouse *KIT* sequences in the GENEBANK database. The RT-PCR products were gel purified and cloned using the pGEM-T vector system (Promega). Plasmid clones were sequenced using a set of internal primers and the ABI Prism™ dRhodamine Terminator Cycle Sequencing Kit (PE Applied Biosystems). Two subclones representing each type of *KIT* sequence were initially sequenced and in those cases where a discrepancy was observed (possibly due to PCR errors) additional clones were sequenced over those particular nucleotide sites. RT-PCR analysis of *KIT* exon 16-19 was carried out with the primers KIT1F (5' – TCR TAC ATA GAA AGA GAY GTG ACT C – 3')(Sequence ID No. 28) and KIT7R (5' – AGC CTT CCT TGA TCA TCT TGT AG – 3')(Sequence ID No. 29).

The paragraph beginning at page 63, line 10 and ending at page 63, line 26 has been amended as follows:

Allelic discrimination reactions were set up using the PE Applied Biosystems TaqMan™ system. 25 µl reactions contained the primers E19FOR (5' – GAGCAGCCCCTACCCCGGAATGCCAGTTGA – 3')(Sequence ID No. 30) and E19REV (5' – CTTTAAAACAGAACATAAAAGCGGAAACATCATGCGAAGG – 3')(Sequence ID No. 31) at 300 nM, 8% glycerol (w/v) 1X TaqMan™ buffer A (PE Applied Biosystems), 5 mM $MgCl_2$, 200 µM dATP, dGTP, dCTP, and dUTP, 0.65 units AmpliTaq Gold™ (PE Applied Biosystems), 0.25 units AmpErase ™ UNG (PE Applied Biosystems) and the TaqMan™ probes E19PC (5' – CATACATTTCCGCAGGTGCATGC – FAM)(Sequence ID No. 52) and E19PT (5' – TCATACATTTCCACAGGTGCATGC – TET)(Sequence ID No. 53) at a concentration of 100 mM. 1 µl of crude lysate DNA was used as template. PCR amplification was carried out using a PE9600 termal cycler (PE Applied Biosystems) or ~~a~~ the ABI7700 Prism (PE Applied Biosystems) with a thermal cycling regime of 50° C for 2 min followed by 95° C for 10 min followed by 40 cycles of 95° C 15 sec, 62° C 1 min. 8 control samples of each homozygote genotype, 2678C and 2678T, and 8 no template controls where deionized water was substituted for template controls were used per 96 well plate. Allele identification based on these reactions was carried out using the allelic discrimination function of the ABI7700 Prism (PE Applied Biosystems).

The paragraph beginning at page 66, line 30 and ending at page 66, line 31 has been amended as follows:

EPIG10 5' – GGT CTA GAT CAC CAG GAG CAC TGC AGC ACC - 3' (Sequence ID No. 32)

EPIG16 5' – GGG AAG CTT GAC CCC CGA GAG CGA CGC GCC - 3' (Sequence ID No. 33)

The paragraphs beginning at page 68, line 22 and ending at page 68, line 34 have been amended as follows:

```
      Pietrain    CGACGCGCCC TCCCTGCTCC CTGGCGGGAC GATGCCTGTG CTTGGCCCGG
      Meishan     ---------- ---------- ---------- ---------- ----------
      Wild Boar   ---------- ---------- ---------- ---------- ----------

      Pietrain    AGAGGAGGCT GCTGGCTTCC CTCAGCTCCG CGCCCCCAGC CGCCCCCCCC
      Meishan     ---------- ---------- ---------- ----------[::] -------::[-
-]-
      Wild Boar   ---------- ---------- ---------- ----------[::] -------::[-
-]-

      Pietrain    GCCTCGGGCT GGCCGCCAAC CAGACCAACC AGACGGGCCC CCAGTGCCTG
      Meishan     ---------- ---------- ---------- ---------- ----------
      Wild Boar   ---------- ---------- ---------- ---------- ----------

      Pietrain    GAGGTGTCCA TT
      Meishan     ---------- --
      Wild Boar   ---------- --
```

These results are also incorporated into figure 1a. The italicized nucleotides of the Pietrain sequence correspond to nucleotides 22 to 30 of EPIG16 (Sequence ID No. 33). The remaining Pietrain sequence shown corresponds to nucleotides 8 to 160 of SEQ ID NO. 39. The Meishan sequence shown corresponds to nucleotides 8 to 158 of SEQ ID NO. 38. The Wild Boar sequence shown corresponds to nucleotides 8 to 158 of SEQ ID NO. 37.

The paragraph beginning at page 69, line 8 and ending at page 69, line 9 has been amended as follows:

MC1R121A 5' – Hex – GGA CTC CAT GGA GCC GCA GAT GAG CAC GGT - 3' (Sequence ID No. 34)

The paragraph beginning at page 70, line 20 and ending at page 70, line 21 has been amended as follows:

EPIG13 5' – GCA AGA CCC TCC AGG AGG TG - 3' (Sequence ID No. 35)

EPIG14 5' – CAC TGA GCC GTA GAA GAG AG - 3' (Sequence ID No. 36)

IN THE CLAIMS

Claims 33 has been amended as follows.

33. The method of claim 32 wherein the gene is the pig α*MSHR* gene and at least one pair of suitable primers is:

αMSHR Forward Primer 1: (5'-TGT AAA ACG ACG GCC AGT RGT GCC TGG AGG TGT CCA T-3')(Sequence ID No. 1) and ;
αMSHR Reverse Primer 5: (5'-CGC CCA GAT GGC CGC GAT GGA CCG-3')(Sequence ID No. 2); or
αMSHR Forward Primer 2: (5'-CGG CCA TCT GGG CGG GCA GCG TGC -3')(Sequence ID No. 3) and
αMSHR Reverse Primer 2: (5'-GGA AGG CGT AGA TGA GGG GGT CCA-3')(Sequence ID No. 4); or
αMSHR Forward Primer 3: (5'-GCA CAT CGC CCG GCT CCA CAA GAC-3')(Sequence ID No. 5) and
αMSHR Reverse Primer 3: (5'-GGG GCA GAG GAC GAC GAG GGA GAG-3')(Sequence ID No. 6).

Claims 46 has been amended as follows.

46. A kit as claimed in claim 45 wherein [the atleast]at least one pair of suitable primers is:

αMSHR Forward Primer 1: (5'-TGT AAA ACG ACG GCC AGT RGT GCC TGG AGG TGT CCA T-3')(Sequence ID No. 1) and
αMSHR Reverse Primer 5: (5'-CGC CCA GAT GGC CGC GAT GGA CCG-3')(Sequence ID No. 2); or

αMSHR Forward Primer 2: (5'-CGG CCA TCT GGG CGG GCA GCG TGC -3')(Sequence ID No. 3) and

αMSHR Reverse Primer 2: (5'-GGA AGG CGT AGA TGA GGG GGT CCA-3')(Sequence ID No. 4); or

αMSHR Forward Primer 3: (5'-GCA CAT CGC CCG GCT CCA CAA GAC-3')(Sequence ID No. 5) and

αMSHR Reverse Primer 3: (5'-GGG GCA GAG GAC GAC GAG GGA GAG-3')(Sequence ID No. 6).

Notice to Comply	Application No.	Applicant(s)	
	09/450,651	ANDERSSON ET AL.	
	Examiner	Art Unit	
	Juliet C. Einsmann	1655	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

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